The American Journal of Pathology, Vol. 176, No. 6, June 2010

DOI: 10.2353/ajpath.2010.100257

This Month in *AJP*

Low Caveolin-1 Expression Contributes to Idiopathic Pulmonary Fibrosis

Low PTEN levels have been implicated in the overproliferation of fibroblasts following tissue injury. However, the molecular mechanisms underlying the low expression of PTEN in lung fibroblasts in idiopathic pulmonary fibrosis (IPF) remain to be determined. Xia et al (**Am J Pathol 2010, 176:2626–2637**) hypothesized that caveolin-1, which is decreased in fibroblasts in IPF patients, may be responsible for the levels of PTEN expression in these cells. They correlated low levels of caveolin-1 and PTEN expression and demonstrated that overexpression of caveolin-1 restored PTEN expression in IPF fibroblasts. Indeed, PTEN interacted with caveolin-1 through its caveolin-1-binding sequence. Decreased caveolin-1 expression therefore facilitates the overproliferation of fibroblasts in IPF.

Antigen-Specific Regulatory Cells Block the Development of Autoimmunity

Antigen-specific effector $CD4^+$ T cells that produce interleukin-17 (Th17 cells) are believed to initiate the inflammatory process in experimental autoimmune encephalitis (EAE), a mouse model of multiple sclerosis. As interferon (IFN)-γ suppresses Th17 cell development, Wildbaum et al (**Am J Pathol 2010, 176:2764–2775**) hypothesized that IFN-γ expressing $CD4^+$ T cells may serve as regulatory cells to block the development of autoimmunity. They discovered that EAE development depended on FasL-mediated apoptosis of these antigen-specific IFN-γ-expressing regulatory cells at early stages of disease and that inhibiting FasL signaling at early stages of EAE suppressed disease development. In addition, overexpression of IFN-γ in EAE-mediating T cells caused them to act instead as antigen-specific regulatory cells. Thus, early suppression of Th17 cells may block the development of autoimmunity.

New Model for Chronic Wasting Disease

Chronic wasting disease is a fatal prion-induced disease that affects cervids such as deer, elk, and moose. Using a mouse model of chronic wasting disease that expresses cervid prion protein (PrP), Seelig et al (**Am J Pathol 2010, 176:2785–2797**) examined the susceptibility, pathogenesis, and transmission of cervid chronic wasting disease. In this model they found that cervid PrP^C (protease-sensitive PrP) was expressed in lymphoid, nervous, hematopoietic, endocrine, and certain epithelial tissues in this model. Additionally, induced spongiform encephalopathy could be transferred by intracerebral, intravenous, intraperitoneal, and oral routes, although the oral route required a larger infecting dose. Furthermore, this disease could be transferred horizontally without experimental intervention to uninfected mice, highlighting the suitability of this system in studying cervid transmissible spongiform encephalopathy.

Inflammasome Increases Muscle Damage in Muscular Dystrophy

Many patients with muscular dystrophy show signs of inflammation; however, the mechanisms governing this inflammation in disease pathogenesis remain unexplored. To investigate the role of the inflammasome in muscular dystrophy, Rawat et al (**Am J Pathol 2010, 176:2891–2900**) examined the inflammasome platform in mouse and human dysferlin-deficient tissues, which develop limb girdle muscular dystrophy type 2B. They found that components of the NALP-3 inflammasome pathway were up-regulated and activated in dysferlin-deficient muscle as compared with control muscle and that primary skeletal muscle cells can secrete interleukin-1β, directly participating in inflammasome formation. Moreover, dysferlin-deficient muscle cells expressed the innate immune molecules Toll-like receptor-2 and -4, suggesting that affected muscle may directly contribute to inflammation in muscular dystrophy and providing a new therapeutic target for limb girdle muscular dystrophy type 2B.

New Target May Inhibit Metastatic Breast Cancer

The pro-apoptotic protein galectin-7 is expressed in and plays a metastatic role in various types of cancer. To determine the role of galectin-7 in breast cancer, Demers et al (**Am J Pathol 2010, 176:3023–3031**) investigated galectin-7 expression and function in these cells. Galectin-7 was highly expressed in two pre-clinical models of breast cancer, and high galectin-7 expression levels increased the metastatic potential of these tumor cells. In humans, high expression levels of galectin-7 were restricted to high-grade tumors and were associated with metastasis. Taken together, these data implicate galectin-7 as both a breast cancer differentiation marker and a potential therapeutic target for metastatic breast cancer.